* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Jul 12	BEILSTEIN enhanced with new display and select options, resulting in a closer connection to BABS
NEWS 4	Jul 30	BEILSTEIN on STN workshop to be held August 24 in conjunction with the 228th ACS National Meeting
NEWS 5	AUG 02	IFIPAT/IFIUDB/IFICDB reloaded with new search and display fields
NEWS 6	AUG 02	CAplus and CA patent records enhanced with European and Japan Patent Office Classifications
NEWS 7	AUG 02	The Analysis Edition of STN Express with Discover! (Version 7.01 for Windows) now available
NEWS 8	AUG 04	Pricing for the Save Answers for SciFinder Wizard within STN Express with Discover! will change September 1, 2004
NEWS 9	AUG 27	BIOCOMMERCE: Changes and enhancements to content coverage
NEWS 10	AUG 27	BIOTECHABS/BIOTECHDS: Two new display fields added for legal status data from INPADOC
NEWS 11	SEP 01	INPADOC: New family current-awareness alert (SDI) available
NEWS 12	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS 13	SEP 01	New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
NEWS 14	SEP 14	STN Patent Forum to be held October 13, 2004, in Iselin, NJ

NEWS EXPRESS	JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:37:22 ON 23 SEP 2004

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 13:37:27 ON 23 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

h eb c g cg b cg eb

```
STRUCTURE FILE UPDATES:    22 SEP 2004  HIGHEST RN 749824-02-0
DICTIONARY FILE UPDATES:   22 SEP 2004  HIGHEST RN 749824-02-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

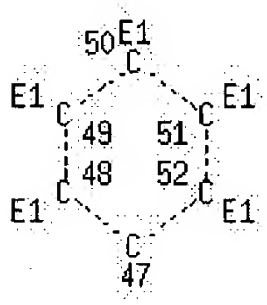
Crossover limits have been increased.  See HELP CROSSOVER for details.

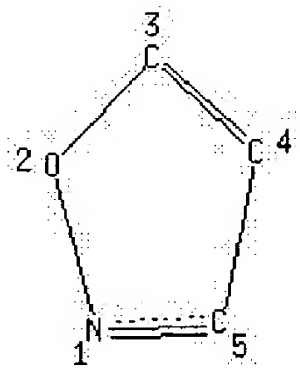
Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1                STR
```

Page 1-B





Page 1-D

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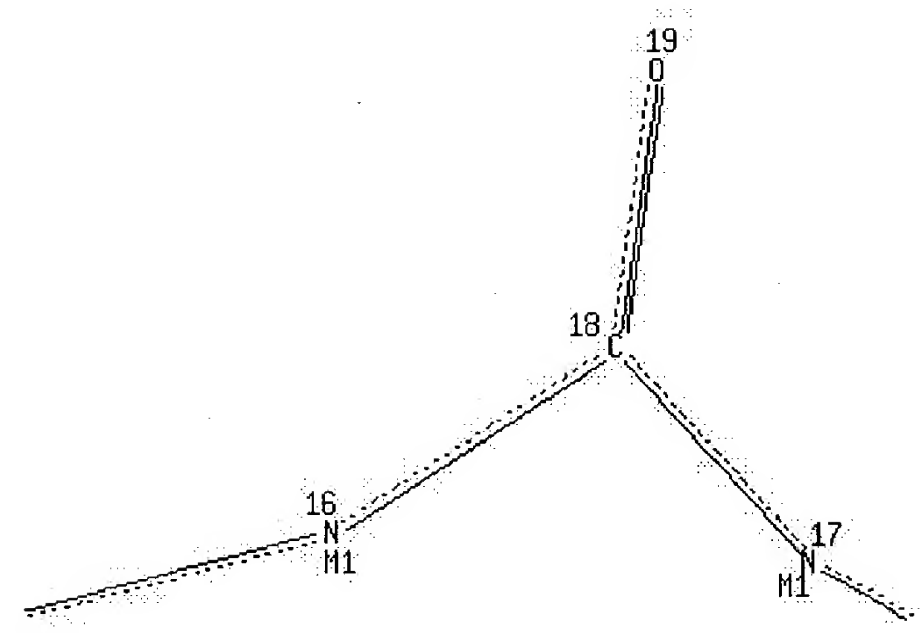
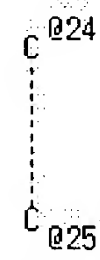
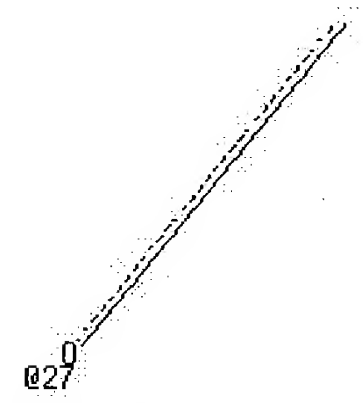


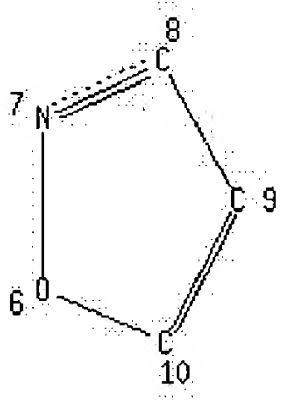
Page 1-E

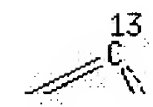


Page 2-A

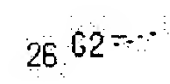


Page 2-B





Page 2-D



Page 2-E

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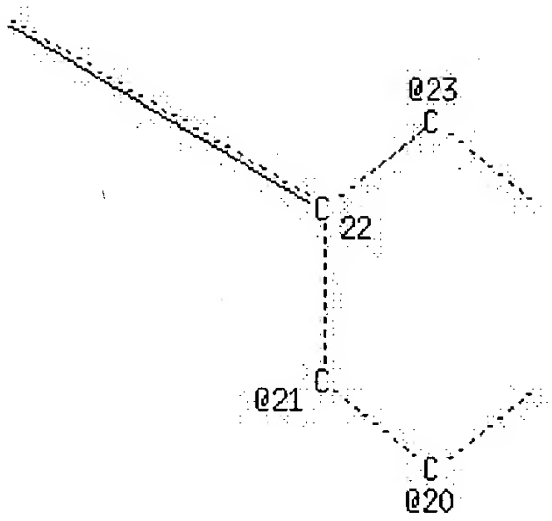

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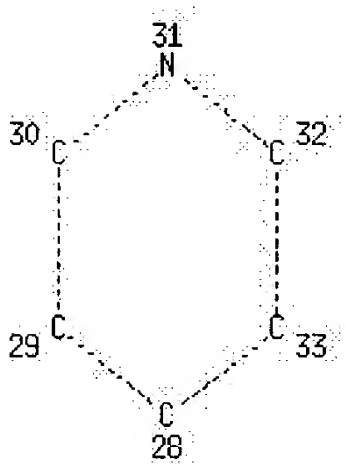
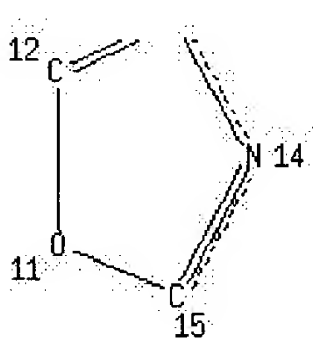


Page 3-B



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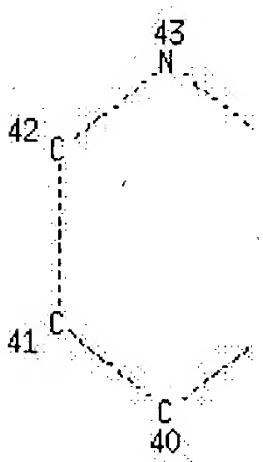

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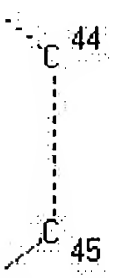
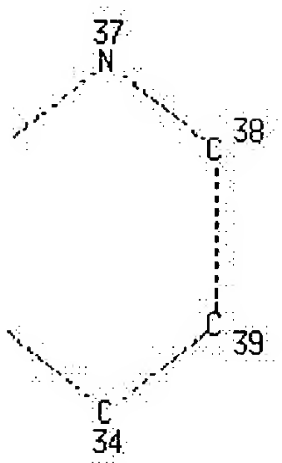


Page 3-F

h eb c g cg b cg eb

Page 4-E



Page 4-F

```
VAR G2=5/10/15
VAR G3=47/34/44
VPA 27-20/21/23/24/25 S
NODE ATTRIBUTES:
HCOUNT   IS M1      AT  16
HCOUNT   IS M1      AT  17
HCOUNT   IS E1      AT  48
HCOUNT   IS E1      AT  49
HCOUNT   IS E1      AT  50
HCOUNT   IS E1      AT  51
HCOUNT   IS E1      AT  52
NSPEC    IS R       AT   1
NSPEC    IS R       AT   2
NSPEC    IS R       AT   3
NSPEC    IS R       AT   4
NSPEC    IS R       AT   5
NSPEC    IS R       AT   6
NSPEC    IS R       AT   7
NSPEC    IS R       AT   8
NSPEC    IS R       AT   9
NSPEC    IS R       AT  10
NSPEC    IS R       AT  11
NSPEC    IS R       AT  12
NSPEC    IS R       AT  13
NSPEC    IS R       AT  14
NSPEC    IS R       AT  15
NSPEC    IS C       AT  16
NSPEC    IS C       AT  17
NSPEC    IS C       AT  18
NSPEC    IS C       AT  19
NSPEC    IS R       AT  20
NSPEC    IS R       AT  21
NSPEC    IS R       AT  22
NSPEC    IS R       AT  23
NSPEC    IS R       AT  24
NSPEC    IS R       AT  25
NSPEC    IS C       AT  26
NSPEC    IS C       AT  27
NSPEC    IS R       AT  28
NSPEC    IS R       AT  29
```

h eb c g cg b cg eb

```
NSPEC   IS R      AT  30
NSPEC   IS R      AT  31
NSPEC   IS R      AT  32
NSPEC   IS R      AT  33
NSPEC   IS R      AT  34
NSPEC   IS R      AT  35
NSPEC   IS R      AT  36
NSPEC   IS R      AT  37
NSPEC   IS R      AT  38
NSPEC   IS R      AT  39
NSPEC   IS R      AT  40
NSPEC   IS R      AT  41
NSPEC   IS R      AT  42
NSPEC   IS R      AT  43
NSPEC   IS R      AT  44
NSPEC   IS R      AT  45
NSPEC   IS C      AT  46
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT  16 17 18 19 27 47 48 49 50 51 52
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  52

STEREO ATTRIBUTES: NONE


=> s l1
SAMPLE SEARCH INITIATED 13:47:16 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            0 TO        0
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 13:47:20 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      6 TO ITERATE

100.0% PROCESSED       6 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

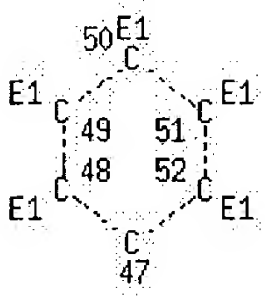
L3            0 SEA SSS FUL L1

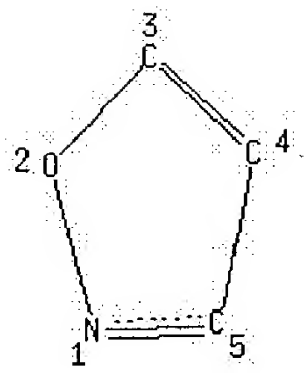
=>
L4      STRUCTURE UPLOADED

=> d l4
L4 HAS NO ANSWERS
L4               STR
```

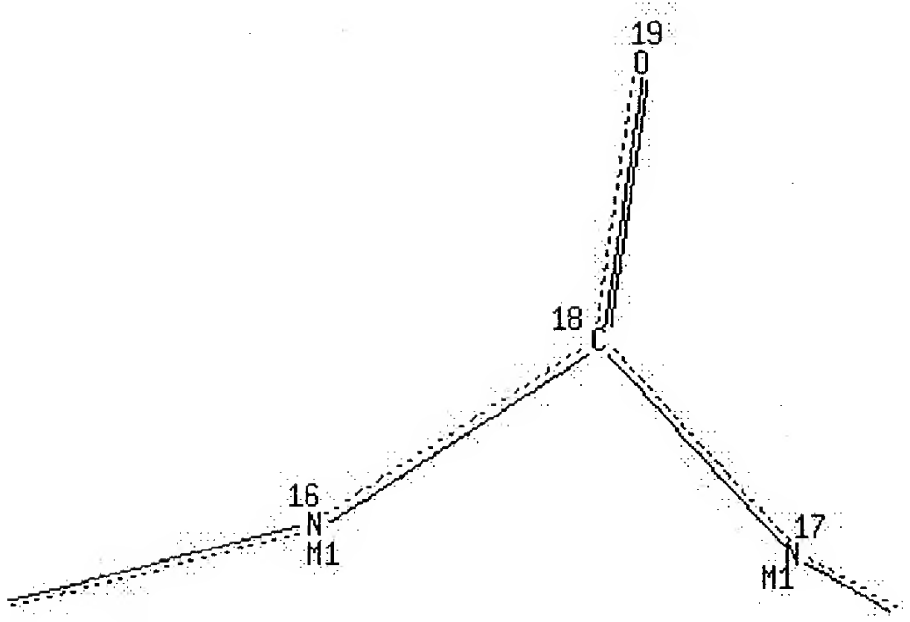
h eb c g cg b cg eb

Page 1-B





Page 1-D



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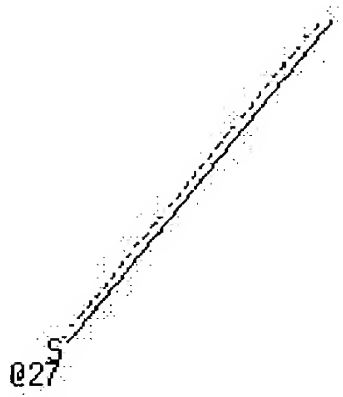
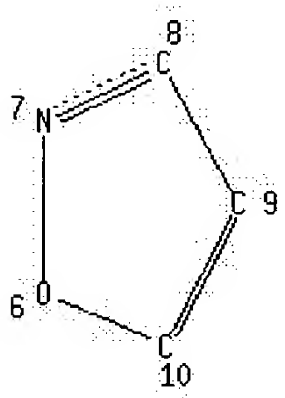
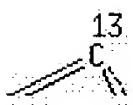
Page 2-A

h eb c g cg b cg eb



Page 2-B





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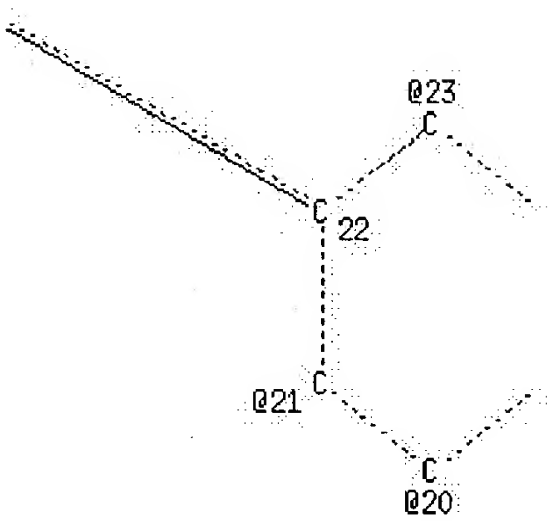
Page 2-E



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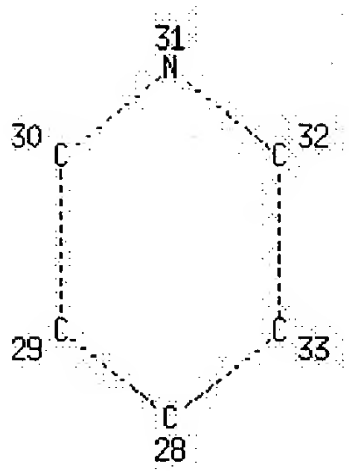
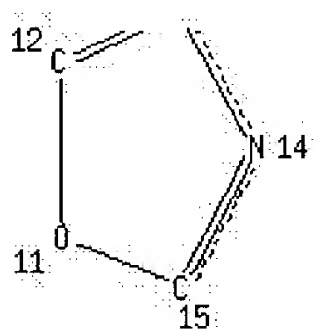
h eb c g cg b cg eb



Page 3-B



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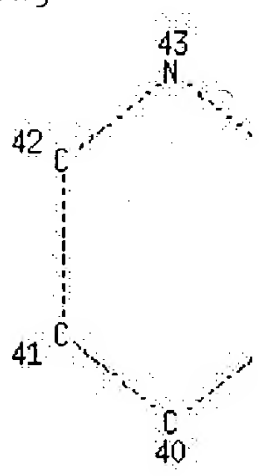

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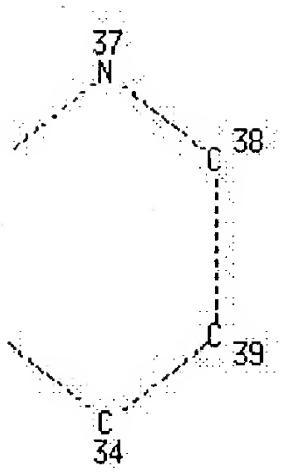
h eb c g cg b cg eb

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Page 4-F
VAR G2=5/10/15
VAR G3=47/34/44
VPA 27-20/21/23/24/25 S
NODE ATTRIBUTES:
HCOUNT  IS M1     AT  16
HCOUNT  IS M1     AT  17
HCOUNT  IS E1     AT  48
HCOUNT  IS E1     AT  49
HCOUNT  IS E1     AT  50
HCOUNT  IS E1     AT  51
HCOUNT  IS E1     AT  52
NSPEC   IS R      AT   1
NSPEC   IS R      AT   2
NSPEC   IS R      AT   3
NSPEC   IS R      AT   4
NSPEC   IS R      AT   5
NSPEC   IS R      AT   6
NSPEC   IS R      AT   7
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NSPEC   IS R      AT  10
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NSPEC   IS R      AT  13
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NSPEC   IS R      AT  15
NSPEC   IS C      AT  16
NSPEC   IS C      AT  17
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NSPEC   IS R      AT  24
NSPEC   IS R      AT  25
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NSPEC   IS R      AT  33
NSPEC   IS R      AT  34
NSPEC   IS R      AT  35
NSPEC   IS R      AT  36
```

h eb c g cg b cg eb

```
NSPEC   IS R      AT  37
NSPEC   IS R      AT  38
NSPEC   IS R      AT  39
NSPEC   IS R      AT  40
NSPEC   IS R      AT  41
NSPEC   IS R      AT  42
NSPEC   IS R      AT  43
NSPEC   IS R      AT  44
NSPEC   IS R      AT  45
NSPEC   IS C      AT  46
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT  16 17 18 19 27 47 48 49 50 51 52
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  52

STEREO ATTRIBUTES: NONE


=> s l4
SAMPLE SEARCH INITIATED 13:47:59 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                          0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:           0 TO        0
PROJECTED ANSWERS:              0 TO        0

L5             0 SEA SSS SAM L4

=> s l4 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 13:48:05 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                          0 ANSWERS
SEARCH TIME: 00.00.01

L6             0 SEA SSS FUL L4

=>
L7      STRUCTURE UPLOADED

=>  l7
L7 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d l7
L7 HAS NO ANSWERS
L7                STR

=> s l7
```

h eb c g cg b cg eb

```
SAMPLE SEARCH INITIATED 13:52:02 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     60 TO ITERATE

100.0% PROCESSED      60 ITERATIONS                          23 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          736 TO     1664
PROJECTED ANSWERS:             173 TO      747

L8            23 SEA SSS SAM L7

=>
L9       STRUCTURE UPLOADED

=> s l9
SAMPLE SEARCH INITIATED 13:58:45 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      8 TO ITERATE

100.0% PROCESSED       8 ITERATIONS                           6 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            8 TO      329
PROJECTED ANSWERS:               6 TO      266

L10           6 SEA SSS SAM L9

=> s l9 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 13:58:51 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    185 TO ITERATE

100.0% PROCESSED     185 ITERATIONS                         135 ANSWERS
SEARCH TIME: 00.00.01

L11          135 SEA SSS FUL L9

=> file hcaplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               480.12     480.33

FILE 'HCAPLUS' ENTERED AT 13:58:54 ON 23 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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```


h eb c g cg b cg eb

FILE COVERS 1907 - 23 Sep 2004 VOL 141 ISS 13
FILE LAST UPDATED: 22 Sep 2004 (20040922/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l11
L12 5 L11

=> s l12 and dumas, j?/au
677 DUMAS, J?/AU
L13 3 L12 AND DUMAS, J?/AU

=> d l13, ibib abs fhitstr, 1-3

L13 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:51821 HCAPLUS
DOCUMENT NUMBER: 140:296858
TITLE: Omega-carboxypyridyl substituted ureas as Raf kinase inhibitors: SAR of the amide substituent
AUTHOR(S): Khire, Uday R.; Bankston, Donald; Barbosa, James; Brittelli, David R.; Caringal, Yolanda; Carlson, Robert; **Dumas, Jacques**; Gane, Todd; Heald, Sarah L.; Hibner, Barbara; Johnson, Jeffrey S.; Katz, Michael E.; Kennure, Nancy; Kingery-Wood, Jill; Lee, Wendy; Liu, Xiao-Gao; Lowinger, Timothy B.; McAlexander, Ian; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Riedl, Bernd; Rong, Hong; Sibley, Robert N.; Smith, Roger A.; Wolanin, Donald
CORPORATE SOURCE: Department of Chemistry Research, Bayer Research Center, West Haven, CT, 06516, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(3), 783-786
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bis-aryl ureas have been disclosed previously as a potent class of Raf kinase inhibitors. Modifications in the amide portion led to an improvement in aq. soly., an important characteristic for an oral drug. Based on this finding, we hypothesize that this portion of the mol. is directed towards the solvent in Raf-1.

IT **228999-58-4**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(structure and Raf kinase inhibitor activity of amide substituent of omega-carboxypyridyl substituted ureas)
RN 228999-58-4 HCAPLUS
CN Benzamide, 3-[4-[[[[5-(1,1-dimethylethyl)-3-isoxazolyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)

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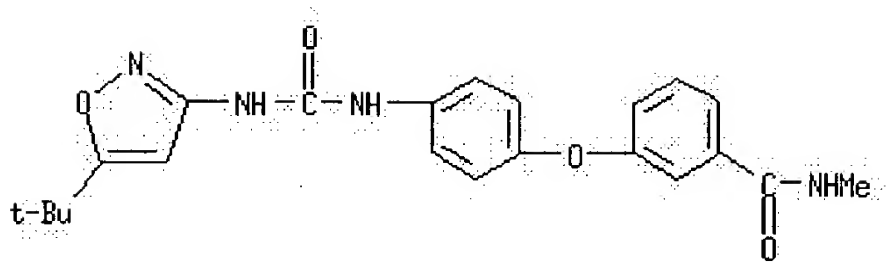

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:425745 HCAPLUS
DOCUMENT NUMBER: 131:87909
TITLE: Inhibition of p38 kinase activity using substituted heterocyclic ureas
INVENTOR(S): **Dumas, Jacques**; Khire, Uday; Lowinger, Timothy Bruno; Paulsen, Holger; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Lee, Wendy; Redman, Aniko
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932111	A1	19990701	WO 1998-US26080	19981222
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RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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AU 739642	B2	20011018		
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JP 2001526223	T2	20011218	JP 2000-525102	19981222
PRIORITY APPLN. INFO.:			US 1997-995750 A	19971222
			WO 1998-US26080 W	19981222

OTHER SOURCE(S): MARPAT 131:87909
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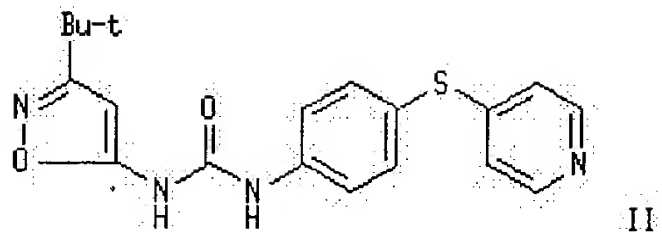


II

AB A method for treatment of p38-mediated disease other than cancer comprises administration of ANHCONHB [I; A = substituted isoxazolyl, pyrazolyl, thienyl, furyl; B = (substituted) mono-, di-, or tricyclic aryl, heteroaryl contg. ≥1 5-6 membered arom. structure contg. 0-4 N, O, or S atoms]. Reaction of 4-(4-pyridinylthio)aniline with 3-tert-butyl-5-isoxazolyl isocyanate in toluene gave title compd. II. In an in vitro p38 kinase assay, I displayed IC50 values of 1-10 μM.

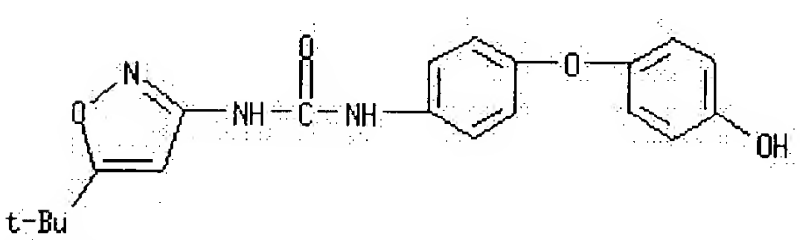
IT **228999-08-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of substituted heterocyclic ureas for treatment of p38 kinase-mediated diseases other than cancer)

RN 228999-08-4 HCAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-3-isoxazolyl]-N'-[4-(4-hydroxyphenoxy)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:425740 HCAPLUS
DOCUMENT NUMBER: 131:73648
TITLE: Inhibition of raf kinase using substituted heterocyclic ureas
INVENTOR(S): **Dumas, Jacques**; Khire, Uday; Lowinger, Timothy Bruno; Paulsen, Holger; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Lee, Wendy; Redman, Aniko
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932106	A1	19990701	WO 1998-US26078	19981222
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TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
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CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2315717	AA	19990701	CA 1998-2315717	19981222
AU 9921989	A1	19990712	AU 1999-21989	19981222
EP 1047418	A1	20001102	EP 1998-965981	19981222
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JP 2001526220	T2	20011218	JP 2000-525097	19981222
BR 9814374	A	20020514	BR 1998-14374	19981222
RU 2232015	C2	20040710	RU 2000-120184	19981222
NO 2000003232	A	20000821	NO 2000-3232	20000621
BG 104597	A	20010228	BG 2000-104597	20000712
PRIORITY APPLN. INFO.:			US 1997-996343 A	19971222
			WO 1998-US26078 W	19981222

OTHER SOURCE(S): MARPAT 131:73648
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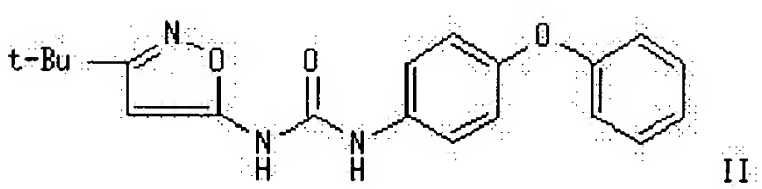
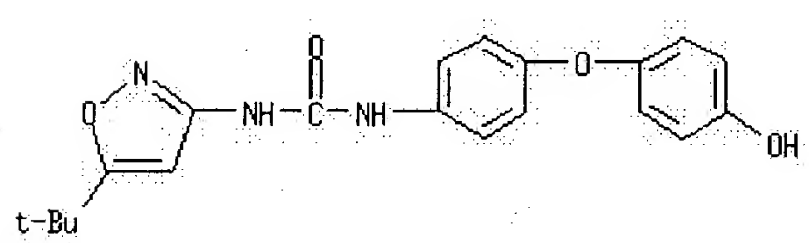


II

AB A method for treatment of cancerous cell growth mediated by raf kinase comprises administration of urea derivs. ANHCONHB [I; A = substituted isoxazolyl, thienyl, thiadiazolyl, furyl, pyrazolyl, etc.; B = (substituted) mono-, di-, or tricyclic aryl, heteroaryl contg. ≥1 5-6 membered arom. structure contg. 0-4 N, O, or S atoms]. Reaction of 4-phenyloxyphenyl isocyanate with 5-amino-3-tert-butylisoxazole in methylene chloride and heating at reflux temp. for 2 days gave title compd. II. In an in vitro raf kinase assay, I displayed IC50 values of 1-10 μM.

IT **228999-08-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of cancerous cell growth mediated by raf kinase)

RN 228999-08-4 HCAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-3-isoxazolyl]-N'-[4-(4-hydroxyphenoxy)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS

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RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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     FILE 'REGISTRY' ENTERED AT 13:37:27 ON 23 SEP 2004
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L17  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

ACCESSION NUMBER: 2001:746592 HCAPLUS
DOCUMENT NUMBER: 136:95577
TITLE: Discovery of heterocyclic ureas as a new class of raf kinase inhibitors: identification of a second generation lead by a combinatorial chemistry approach
AUTHOR(S): Smith, R. A.; Barbosa, J.; Blum, C. L.; Bobko, M. A.; Caringal, Y. V.; Dally, R.; Johnson, J. S.; Katz, M. E.; Kennure, N.; Kingery-Wood, J.; Lee, W.; **Lowinger, T. B.**; Lyons, J.; Marsh, V.; Rogers, D. H.; Swartz, S.; Walling, T.; Wild, H.
CORPORATE SOURCE: Department of Chemistry Research, Bayer Research Center, West Haven, CT, 06516, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(20), 2775-2778
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal

h eb c g cg b cg eb

LANGUAGE: English

AB Heterocyclic ureas, such as N-3-thienyl N'-aryl ureas, have been identified as novel inhibitors of raf kinase, a key mediator in the ras signal transduction pathway. Structure-activity relationships were established, and the potency of the screening hit was improved 10-fold to IC50=1.7 μM. A combinatorial synthesis approach enabled the identification of a breakthrough lead (IC50=0.54 μM) for a second generation series of heterocyclic urea raf kinase inhibitors.

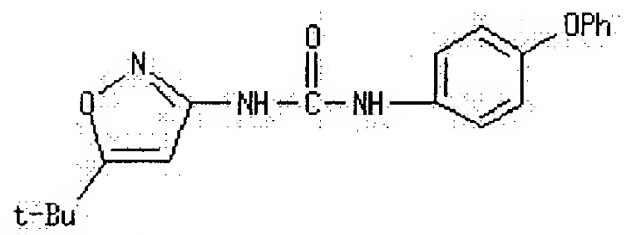
IT **228998-90-1P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(heterocyclic ureas as raf kinase inhibitors)

RN 228998-90-1 HCAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-3-isoxazolyl]-N'-(4-phenoxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

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L6              0 S L4 FULL
L7                STRUCTURE UPLOADED
L8             23 S L7
L9                STRUCTURE UPLOADED
L10             6 S L9
L11           135 S L9 FULL

     FILE 'HCAPLUS' ENTERED AT 13:58:54 ON 23 SEP 2004
L12             5 S L11
L13             3 S L12 AND DUMAS, J?/AU
L14             2 S L12 NOT L13
L15             0 S L14 AND KHIRE, U?/AU
L16             4 S L12 AND LOWINGER, T?/AU
L17             1 S L16 NOT L13

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FILE 'REGISTRY' ENTERED AT 14:00:55 ON 23 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   22 SEP 2004  HIGHEST RN 749824-02-0
DICTIONARY FILE UPDATES:  22 SEP 2004  HIGHEST RN 749824-02-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
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FILE COVERS 1907 - 23 Sep 2004  VOL 141 ISS 13
FILE LAST UPDATED: 22 Sep 2004  (20040922/ED)

 This file contains CAS Registry Numbers for easy and accurate
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L23  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Refarences

ACCESSION NUMBER: 1999:425745 HCAPLUS
DOCUMENT NUMBER: 131:87909
TITLE: Inhibition of p38 kinase activity using substituted heterocyclic ureas
INVENTOR(S): **Dumas, Jacques**; Khire, Uday; Lowinger, Timothy Bruno; Paulsen, Holger; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Lee, Wendy; Redman, Aniko
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932111	A1	19990701	WO 1998-US26080	19981222
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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AU 9919971	A1	19990712	AU 1999-19971	19981222
AU 739642	B2	20011018		
EP 1041982	A1	20001011	EP 1998-964709	19981222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001526223	T2	20011218	JP 2000-525102	19981222
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OTHER SOURCE(S): MARPAT 131:87909
GI

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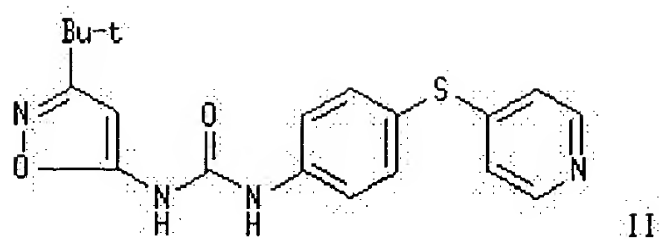


II

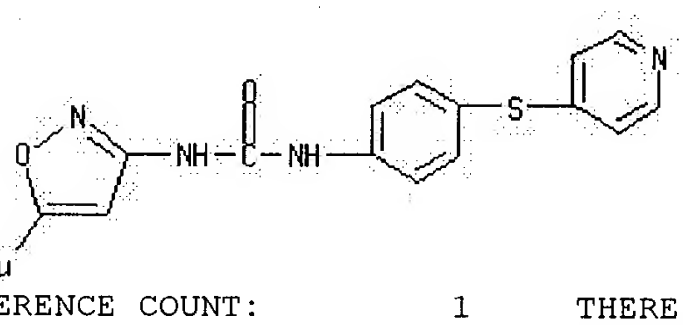
AB A method for treatment of p38-mediated disease other than cancer comprises administration of ANHCONHB [I; A = substituted isoxazolyl, pyrazolyl, thienyl, furyl; B = (substituted) mono-, di-, or tricyclic aryl, heteroaryl contg. ≥1 5-6 membered arom. structure contg. 0-4 N, O, or S atoms]. Reaction of 4-(4-pyridinylthio)aniline with 3-tert-butyl-5-isoxazolyl isocyanate in toluene gave title compd. II. In an in vitro p38 kinase assay, I displayed IC50 values of 1-10 μM.

IT **228999-10-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of p38 kinase-mediated diseases other than cancer)

RN 228999-10-8 HCAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-3-isoxazolyl]-N'-[4-(4-pyridinylthio)phenyl]- (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:425740 HCAPLUS
DOCUMENT NUMBER: 131:73648
TITLE: Inhibition of raf kinase using substituted heterocyclic ureas
INVENTOR(S): **Dumas, Jacques**; Khire, Uday; Lowinger, Timothy Bruno; Paulsen, Holger; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Lee, Wendy; Redman, Aniko
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932106	A1	19990701	WO 1998-US26078	19981222
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MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2315717	AA	19990701	CA 1998-2315717		19981222
AU 9921989	A1	19990712	AU 1999-21989		19981222
EP 1047418	A1	20001102	EP 1998-965981		19981222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
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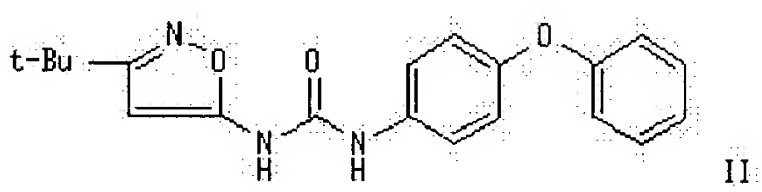
JP 2001526220	T2	20011218	JP 2000-525097		19981222
BR 9814374	A	20020514	BR 1998-14374		19981222
RU 2232015	C2	20040710	RU 2000-120184		19981222
NO 2000003232	A	20000821	NO 2000-3232		20000621
BG 104597	A	20010228	BG 2000-104597		20000712
PRIORITY APPLN. INFO.:			US 1997-996343	A	19971222
			WO 1998-US26078	W	19981222

OTHER SOURCE(S): MARPAT 131:73648
GI



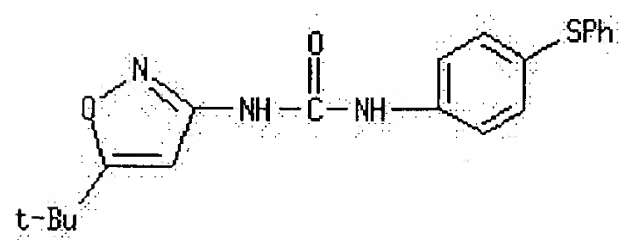
II

AB A method for treatment of cancerous cell growth mediated by raf kinase comprises administration of urea derivs. ANHCONHB [I; A = substituted isoxazolyl, thienyl, thiadiazolyl, furyl, pyrazolyl, etc.; B = (substituted) mono-, di-, or tricyclic aryl, heteroaryl contg. ≥1 5-6 membered arom. structure contg. 0-4 N, O, or S atoms]. Reaction of 4-phenyloxyphenyl isocyanate with 5-amino-3-tert-butylisoxazole in methylene chloride and heating at reflux temp. for 2 days gave title compd. II. In an in vitro raf kinase assay, I displayed IC50 values of 1-10 μM.

IT **228998-97-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of cancerous cell growth mediated by raf kinase)

RN 228998-97-8 HCAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-3-isoxazolyl]-N'-[4-(phenylthio)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L11           135 S L9 FULL

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L24  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

ACCESSION NUMBER: 2002:107924 HCAPLUS
DOCUMENT NUMBER: 136:167692
TITLE: Preparation of new biphenyl and biphenyl-analogous compounds as integrin antagonists
INVENTOR(S): Albers, Markus; Urbahns, Klaus; Vaupel, Andrea; Harter, Michael; Schmidt, Delf; Stelte-Ludwig, Beatrix; Gerdes, Christoph; Stahl, Elke; Keldenich, Jorg; Brueggemeier, Ulf; Lustig, Klemens
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: U.S. Pat. Appl. Publ., 256 pp., Division of U.S. Ser. No. 464,237.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002016461	A1	20020207	US 2001-828514		20010406
US 6677360	B2	20040113			
US 6420396	B1	20020716	US 1999-464237		19991215
US 2004030132	A1	20040212	US 2002-285073		20021031
PRIORITY APPLN. INFO.:			US 1998-172225P	P	19981216
			US 1999-464237	A3	19991215
			US 1999-172217P	P	19991019
			US 2001-828514	A3	20010406

OTHER SOURCE(S): MARPAT 136:167692

AB Biphenylyl compds. R1O2CCHR2-U-V-A-B-W-NR3-C-R4 [R1 = H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl; R2 = H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl, alkenyl, alkynyl, -NR2'SO2R2'', -NR2'CO2R2', -NR2'COR2', -NR2'CONR2'2, -NR2'CSNR2'2 (R2' has same definition as R1 and R2'' has same definition as R1 except it is not H); U or W is a direct bond or (un)substituted alkylene; V = (un)substituted alkylene, -NR2'CO- or NR2'SO2-; A and B =

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(un)substituted 1,3- or 1,4-bridging phenylene group or a 2,4- or 2,5-bridging thienylene group, each of which may have substituents; C is a direct bond, CMe(:X-R5)-Y-N(R6)- (R5 is absent, H, (un)substituted alkyl or cycloalkyl, NO2, acyl, carboxylic or carboxylate group or is connected to R3, Y, R4 or R6, if present; R6 is H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl, an alkylamine or alkylamide residue, or is connected to one of R3, R4, Y, or R5, if present, to form a heterocyclic ring system; X = CHNO2, CHCN, O, N or S; Y is a direct bond or (un)substituted alkylene or alkyne group) or 3,4-dioxo-1,2-cyclobutenediyl-NR6-; R3, R4 = H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl, an alkylamine or alkylamide residue, or is connected to one of R4 (or R3), Y, R5 or R6, if present, to form a heterocyclic ring system] were prepd. as integrin antagonists. For example, (2R,S)-3-[3-(pyridin-3-ylmethylureido)biphenyl-4-yl]-2-[2,4,6-trimethylbenzenesulfonylamino]propanoic acid, prepd. by reactions of resin-bound (2R,S)-3-(4-bromophenyl)-2-(9-fluorenylmethoxycarbonylamino)propanoic acid with sulfonylating, boronic acid, and amine reagents (mesitylenesulfonyl chloride, 3-nitrobenzeneboronic acid, and 2-aminomethylpyridine), showed IC50 = 5 nM for binding to the αvβ3 receptor and IC50 = 480 nM in the smooth muscle cell migration test. Thus, the invention compds. are useful for the inhibition of angiogenesis and/or for therapy and prophylaxis of cancer, osteolytic diseases such as osteoporosis, arteriosclerosis, restenosis, rheumatoid arthritis, and ophthalmic disorders (no data).

IT **276261-89-3P**

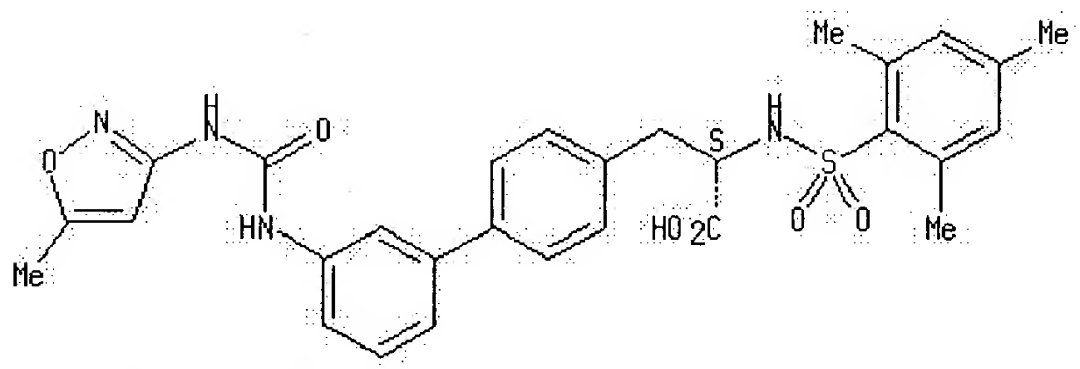
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of biphenyl amino acid analogs as integrin antagonists for inhibition of angiogenesis and treatment of cancer, osteolytic diseases, arteriosclerosis, restenosis, rheumatoid arthritis, and ophthalmic disorders)

RN 276261-89-3 HCAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, 3'-[[[(5-methyl-3-isoxazolyl)amino]carbonyl]amino]-α-[[(2,4,6-trimethylphenyl)sulfonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:421093 HCAPLUS

DOCUMENT NUMBER: 133:43809

TITLE: Preparation of new biphenyl and biphenyl-analogous compounds as integrin antagonists

INVENTOR(S): Albers, Markus; Urbahns, Klaus; Vaupel, Andrea; Harter, Michael; Schmidt, Delf; Stelte-ludwig, Beatrix; Gerdes, Christoph; Stahl, Elke; Keldenich,

h eb c g cg b cg eb

Jorg; Bruggemeier, Ulf; Lustig, Klemens
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany; et al.
SOURCE: PCT Int. Appl., 360 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035864	A1	20000622	WO 1999-EP9843	19991213
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ZA 2001014432	A	20020530	ZA 2001-14432	20010530
BG 105574	A	20020131	BG 2001-105574	20010607
NO 2001002975	A	20010813	NO 2001-2975	20010615
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PRIORITY APPLN. INFO.:			US 1998-213381 A	19981216
			WO 1999-EP9843 W	19991213

OTHER SOURCE(S): MARPAT 133:43809

AB Biphenylyl compds. R1O2CCHR2-U-V-A-B-W-NR3-C-R4 [R1 = H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl; R2 = H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl, alkenyl, alkynyl, -NR2'SO2R2'', -NR2'CO2R2', -NR2'COR2', -NR2'CONR2'2, -NR2'CSNR2'2 (R2' has same definition as R1 and R2'' has same definition as R1 except it is not H); U or W is a direct bond or (un)substituted alkylene; V = (un)substituted alkylene, -NR2'CO- or NR2'SO2-; A and B = (un)substituted 1,3- or 1,4-bridging phenylene group or a 2,4- or 2,5-bridging thienylene group, each of which may have substituents; C is a direct bond, CMe(:X-R5)-Y-N(R6)- (R5 is absent, H, (un)substituted alkyl or cycloalkyl, NO2, acyl, carboxylic or carboxylate group or is connected to R3, Y, R4 or R6, if present; R6 is H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl, an alkylamine or alkylamide residue, or is connected to one of R3, R4, Y, or R5, if present, to form a heterocyclic ring system; X = CHNO2, CHCN, O, N or S; Y is a direct bond or (un)substituted alkylene or alkyne group) or 3,4-dioxo-1,2-cyclobutenediyl-NR6-; R3, R4 = H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl, an alkylamine or alkylamide residue, or is connected to one of R4 (or R3), Y, R5 or R6, if present, to form a heterocyclic ring system] were prepd. as integrin antagonists. Thus, (2R,S)-3-[3-(pyridin-3-ylmethylureido)biphenyl-4-yl]-2-[2,4,6-trimethylbenzenesulfonylamino]propanoic acid, prepd. by reactions of resin-bound (2R,S)-3-(4-bromophenyl)-2-(9-fluorenylmethoxycarbonylamino)pr

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opanoic acid with sulfonylating, boronic acid, and amine reagents (mesitylenesulfonyl chloride, 3-nitrobenzeneboronic acid, and 2-aminomethylpyridine), showed IC50 = 5 nM for binding to the αvβ3 receptor and IC50 = 480 nM in the smooth muscle cell migration test.

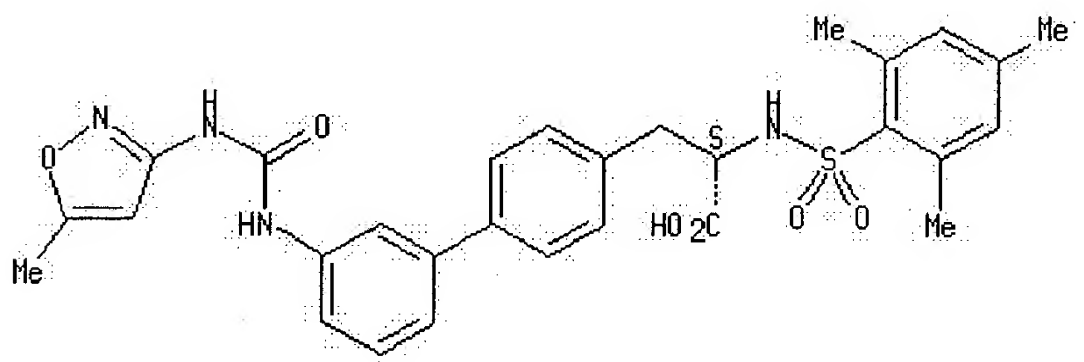
IT **276261-89-3P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of new biphenyl and biphenyl-analogous compds. as integrin antagonists)

RN 276261-89-3 HCAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, 3'-[[[(5-methyl-3-isoxazolyl)amino]carbonyl]amino]-α-[[(2,4,6-trimethylphenyl)sulfonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

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